# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

LEE et al.

Atty. Ref.: 1498-121

Serial No. 09/786,521

Group: 1634

Filed: March 6, 2001

Examiner: Whisenant

For: METHOD FOR MONITORING THE TEMPERATURE OF A BIOCHEMICAL REACTION

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December 18, 2002

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

## AMENDMENT

Responsive to the Official Action dated September 27, 2002, please amend the above-identified application as follows:

## IN THE CLAIMS

Cancel claim 2.

Please substitute the following amended claims for corresponding claims previously presented. A copy of the amended claims showing current revisions is attached.

1. (Amended) A method of monitoring the temperature of a biochemical reaction in a reaction mixture, said method comprising effecting the reaction in the presence of a fluorescently labelled temperature probe DNA sequence which comprises a double stranded region which denatures at a predetermined temperature, the fluorescent label of said temperature probe sequence being arranged so that a detectable signal occurs at the point at which denaturation of the said region takes place; and monitoring fluorescence from said reaction mixture so as to determine when the said predetermined temperature has been reached.

6. (Amended) A method according to claim 1 or claim 3 wherein the fluorescent label uses fluorescence resonance transfer (FRET) as the basis of the signal.

9. (Amended) A method according to claim 7 wherein the reporter and quencher molecules are located on different strands of a DNA temperature probe sequence such that on hybridisation of the strands, they are brought into close proximity to each other.

12. (Amended) A method according to claim 1 wherein the length of the temperature probe sequence is used to set the said predetermined temperature.

13. (Amended) A method according to claim 1 wherein the GC content of the temperature probe sequence is modified to obtain the desired predetermined temperature.

14. (Amended) A method according to claim 1 wherein the biochemical reaction is an amplification reaction.

Furthermore, Hiyoshi, Ririe and Tyagi do not disclose a method wherein a double stranded region denatures at a predetermined temperature. The denaturing temperature of the double stranded region in Hiyoshi, Ririe and Tyagi is not predetermined, i.e. the temperature has not been determined or measured beforehand. In Hiyoshi, Ririe and Tyagi this temperature is unknown and in any event it is not important that this temperature is known for the purposes of the cited prior art documents. Hiyoshi, Ririe and Tyagi merely use the change in fluorescence to indicate that a particular stage of a reaction has been reached.

In claim 1 of the present application, the denaturing temperature of the double stranded region is predetermined, i.e. it is known with accuracy. Hence, on denaturing of this region the temperature of the reaction mixture is accurately known. This is not the case in Hiyoshi, Ririe and Tyagi.

Furthermore, Livak merely teaches that one can measure temperatures of biochemical reactions.

Hence, the combination of the method of any of Hiyoshi, Ririe and Tyagi in combination with the teaching of Livak does not render the solution of claim 1 obvious to a person skilled in this art.

For the above reasons it is respectfully submitted that the claims of this application define inventive subject matter. Reconsideration and allowance are solicited.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages is captioned "**Version With Markings To Show Changes Made.**"

Respectfully submitted,

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